Patent
261/011

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:	Group Art Unit: 1631
Michael J. Heller et al.	Examiner: Marschel
Serial No.: Not Yet Assigned	
Filed: July 24, 2001	
For: Methods for Electronic Synthesis of Complex Structures (as amended herein)	

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

Sir:

Please amend the application as follows:

IN THE TITLE:

Please change the title to "Methods for Electronic Synthesis of Complex Structures".

OC-87972.1

CERTIFICATE OF MAILING
(37 C.F.R. §1.10)

I hereby certify that this paper (along with any referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as 'Express Mail Post Office To Addressee' in an envelope addressed to the Commissioner for Patents, Washington, D.C. 20231.

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IN THE SPECIFICATION:

Page 1, line 1, please insert:

RELATED APPLICATION INFORMATION

This application is a continuation of U.S. Serial No. 09/490,965, filed January 24, 2000, which is a continuation of U.S. Serial No. 08/271,882, filed July 7, 1994, now issued as U.S. Patent No. 6,017,696, which is a continuation-in-part of U.S. Serial No. 08/146,504, filed November 1, 1993, now issued as U.S. Patent No. 5,605,662.

IN THE CLAIMS:

Please cancel claims 1-94.

Please add the following new claims 95-213:

95. A method for electronic synthesis of a plurality of complex structures on a substrate, comprising the steps of:

providing a substrate having a plurality of controllable electrodes supported by the substrate,

providing first structures coupled to the electrodes, the structures having a blocked functional group,

providing a solution in contact with the array of electrodes,

applying a potential to selected electrodes where synthesis is to occur in order to cause deblocking of the first structure,

reacting a second structure with the deblocked first structure, and

repeating the steps of deblocking and reacting another structure to form the plurality of complex structures.

96. The method of claim 95 wherein the complex structures include a nanostructure.

97. The method of claim 95 wherein the complex structure include a polymer.

98. The method of claim 95 wherein the polymer is a synthetic polymer.

99. The method of claim 95 wherein the polymer is a biopolymer.

100. The method of claim 99 wherein the biopolymer is a polynucleotide.

101. The method of claim 99 wherein the biopolymer is a peptide.

102. The method of claim 95 wherein the first structure is a nucleotide.

103. The method of claim 95 wherein the first structure is a nanostructure.

104. The method of claim 95 wherein the first structure is a monomer.

105. The method of claim 95 wherein the first structure is an amino acid.

106. The method of claim 95 wherein the first structure is a chemically reactive moeity.

107. The method of claim 95 wherein the electrodes have terminal portions formed in an array.

108. The method of claim 95 wherein the synthesis of the plurality of complex structures occurs without mechanical movement of electrodes.

109. The method of claim 95 further including providing a layer of material disposed adjacent the electrodes.

110. The method of claim 109 wherein the layer couples the first structure to the electrode.

111. The method of claim 109 wherein the layer comprises a mesh structure.

112. The method of claim 109 wherein the layer comprises a porous structure.

113. The method of claim 109 wherein the layer comprises a lawn structure.

114. The method of claim 109 wherein the layer is a monolayer.

115. The method of claim 95 further including providing a scavenging substance.

116. The method of claim 115 wherein the scavenging substance is included in a layer of material disposed adjacent the electrode.

117. The method of claim 115 wherein the scavenging substance scavenges adverse materials.

118. The method of claim 117 wherein the adverse materials are produced in an electrochemical reaction.

119. The method of claim 109 wherein the layer is a permeation layer.

120. The method of claim 109 further including a first structure coupled to the layer.

121. The method of claim 95 wherein the second structure is present at the time of deblocking of the first structure.

122. The method of claim 95 wherein the second structure is provided subsequent to the deblocking of the first structure.

123. The method of claim 95 wherein the application of the potential to the selected electrodes causes electrophoretic transport of charged reactants to where synthesis is to occur.

124. The method of claim 95 further including the step of providing a charged deblocking reagent which is selectively attracted adjacent an electrode.

125. The method of claim 124 wherein the charged deblocking reagent is electrophoretically transported to an electrode.

126. The method of claim 95 wherein the electrodes are formed directly on the substrate.

127. The method of claim 95 wherein the electrodes are round.

128. The method of claim 95 wherein the electrodes are planar.

129. The method of claim 95 wherein a second potential is applied to at least one other electrode to protect structures at selected locations.

130. The method of claim 129 wherein the protected selected structure is associated with the electrode having the second potential.

131. The method of claim 95 wherein the electrode array is in contact with a common solution.

132. The method of claim 95 wherein the sequence of the structure of the array is determined by selective activation of electrodes adjacent a common solution.

133. The method of claim 95 wherein the application of an electric field to the selected electrodes provides a local concentration of reagents, wherein the reagents activate the selected site.

134. The method of claim 133 wherein activation of the selected site includes deblocking of the selected site.

135. The method of claim 95 wherein the electric field causes increased local concentration of reagents at the sites where the sub-unit is to be coupled.

136. The method of claim 95 wherein the solution contains a phosphate buffer.

137. The method of claim 95 wherein the solution contains a citrate buffer.

138. The method of claim 95 wherein the solution contains a borate buffer.

139. The method of claim 95 wherein the solution contains a TRIS buffer.

140. The method of claim 95 wherein the solution contains a TBE buffer.

141. The method of claim 95 wherein the functional group is a chemical functional group.

142. A method for electronic synthesis of an array of separately formed polymers on a substrate, which comprises the steps of:

placing a buffering solution in contact with an array of electrodes that is proximate to a substrate surface, said surface being proximate to one or more molecules bearing at least one protected chemical functional group attached thereto,

selectively deprotecting at least one protected chemical functional group on at least one of said molecules;

bonding a first monomer having at least one protected chemical functional group to one or more deprotected chemical functional groups of said molecule;

selectively deprotecting a chemical functional group on the bonded molecule or another of said molecules bearing at least one protected chemical functional group;

bonding a second monomer having at least one protected chemical functional group to a deprotected chemical functional group of the bonded molecule or said other deprotected molecule; and

repeating the selective deprotection of a chemical functional group on a bonded protected monomer or a bonded protected molecule and the subsequent bonding of an additional monomer to said deprotected chemical functional group until at least two separate polymers of desired length are formed on the substrate surface.

143. A method according to claim 142, wherein said buffering solution is selected from borate buffers, citrate buffers, and phosphate buffers.

144. A method according to claim 142, wherein said buffering solution is present in a concentration of at least 0.01 mM.

145. A method according to claim 142, wherein the concentration of the buffering solution ranges from 0.1 to 100 mM.

146. A method according to claim 142, wherein said monomers are amino acids.

147. A method according to claim 142, wherein said molecules are linker molecules or monomers.

148. A method according to claim 142, wherein said molecules are attached to a layer of material overlaying said substrate surface.

149. A method according to claim 142, wherein said substrate is formed from at least one material selected from semiconductors, glass, ceramics and polymers.

150. A method according to claim 142, wherein said array of electrodes comprises at least 100 electrodes.

151. A method according to claim 150, wherein said array of electrodes comprises a matrix having hundreds of thousands of electrodes.

152. A method according to claim 142, wherein each of the electrodes in said array ranges in diameter from less than 0.5 micron to about 200 microns.

153. A method according to claim 142, wherein the electrodes of said array are formed from platinum or palladium.

154. A method according to claim 142, which further comprises an additional bonding step wherein a pre-formed molecule is bonded to a deprotected chemical functional group on one or more of said molecules or monomers.

155. The method according to claim 142 wherein the monomer is a nucleotide.

156. A method according to claim 142 wherein a structure which scavenges adverse materials produced in an electrolysis reaction is situated proximate to one or more of said electrodes.

157. A method for electronically controlled synthesis of a plurality of complex structures on a substrate, comprising the steps of:

providing a substrate having a plurality of controllable electrodes supported by the substrate and covered with a non-insulating layer,

providing first structures coupled to the electrodes, the structures having a protected functional group,

providing a solution in contact with the array of electrodes supported by the substrate,

applying a potential to selected electrodes where synthesis is to occur,

reacting a second structure with the first structure, and

repeating the step of applying a potential and reacting a subsequent structure to form the complex structures, the synthesis of the array of structures occuring without mechanical movement.

158. The method of claim 157 wherein the activating of the selected site includes the deblocking of a protected reaction group.

159. The method of claim 157 wherein the complex structures include a nanostructure.

160. The method of claim 157 wherein the complex structure include a polymer.

161. The method of claim 157 wherein the polymer is a synthetic polymer.

162. The method of claim 157 wherein the polymer is a biopolymer.

163. The method of claim 162 wherein the biopolymer is a polynucleotide.

164. The method of claim 162 wherein the biopolymer is a peptide.

165. The method of claim 157 wherein the first structure is a nucleotide.

166. The method of claim 157 wherein the first structure is a nanostructure.

167. The method of claim 157 wherein the first structure is a monomer.

168. The method of claim 157 wherein the first structure is an amino acid.

169. The method of claim 157 wherein the first structure is a chemically reactive moeity.

170. The method of claim 157 wherein the electrodes have terminal portions formed in an array.

171. The method of claim 157 wherein the synthesis of the plurality of complex structures occurs without mechanical movement of electrodes.

172. The method of claim 157 further including providing a layer of material disposed adjacent the electrodes.

173. The method of claim 172 wherein the layer couples the first structure to the electrode.

174. The method of claim 172 wherein the layer comprises a mesh structure.

175. The method of claim 172 wherein the layer comprises a porous structure.

176. The method of claim 172 wherein the layer comprises a lawn structure.

177. The method of claim 172 wherein the layer is a monolayer.

178. The method of claim 157 further including providing a scavenging substance.

179. The method of claim 178 wherein the scavenging substance is included in a layer of material disposed adjacent the electrode.

180. The method of claim 178 wherein the scavenging substance scavenges adverse materials.

181. The method of claim 180 wherein the adverse materials are produced in an electrochemical reaction.

182. The method of claim 172 wherein the layer is a permeation layer.

183. The method of claim 172 further including a first structure coupled to the layer.

184. The method of claim 157 wherein the second structure is present at the time of deblocking of the first structure.

185. The method of claim 157 wherein the second structure is provided subsequent to the deblocking of the first structure.

186. The method of claim 157 wherein the application of the potential to the selected electrodes causes electrophoretic transport of charged reactants to where synthesis is to occur.

187. The method of claim 157 further including the step of providing a charged deblocking reagent which is selectively attracted adjacent an electrode.

188. The method of claim 187 wherein the charged deblocking reagent is electrophoretically transported to an electrode.

189. The method of claim 157 wherein the electrodes are formed directly on the substrate.

190. The method of claim 157 wherein the electrodes are round.

191. The method of claim 157 wherein the electrodes are planar.

192. The method of claim 157 wherein a second potential is applied to at least one other electrode to protect structures at selected locations.

193. The method of claim 192 wherein the protected selected structure is associated with the electrode having the second potential.

194. The method of claim 157 wherein the electrode array is in contact with a common solution.

195. The method of claim 157 wherein the sequence of the structure of the array is determined by selective activation of electrodes adjacent a common solution.

196. The method of claim 157 wherein the application of an electric field to the selected electrodes provides a local concentration of reagents, wherein the reagents activate the selected site.

197. The method of claim 196 wherein activation of the selected site includes deblocking of the selected site.

198. The method of claim 157 wherein the electric field causes increased local concentration of reagents at the sites where the sub-unit is to be coupled.

199. The method of claim 157 wherein the solution contains a phosphate buffer.

200. The method of claim 157 wherein the solution contains a citrate buffer.

201. The method of claim 157 wherein the solution contains a borate buffer.

202. The method of claim 157 wherein the solution contains a TRIS buffer.

203. The method of claim 157 wherein the solution contains a TBE buffer.

204. The method of claim 157 wherein the functional group is a chemical functional group.

205. A method for electronically controlled synthesis of an array of structures supported on a substrate, the synthesized structures including a predetermined sequence of sub-units, comprising the steps of:

providing an plurality of electrodes, the electrodes being supported by the substrate,

providing a buffer in contact with the electrodes,

applying an electric field to selected electrodes wherein a sub-unit is to be included within the structures of the array and applying a second electric field to at least certain other selected electrodes to protect the structures within the array where the said sub-unit is not to be included, and

coupling a selected sub-unit to the said selected locations within the array wherein the sub-unit is to be included.

206. The method of claim 205 wherein the synthesis of the array of structures occurs without mechanical movement of the electrodes.

207. A method for electronically controlled synthesis of a plurality of complex structures on a substrate, comprising the steps of:

providing a substrate having a plurality of controllable electrodes supported by the substrate and covered with a non-insulating layer,

providing first structures coupled to the electrodes, the structures having a blocking group,

providing a first solution in contact with the array of electrodes supported by the substrate containing an enzyme for selective removal of the blocking group,

applying a potential to selected electrodes where synthesis is to occur, thereby concentrating the enzyme at those selected sites,

providing a second solution containing a second enzyme for coupling and a second structure having a blocking group in contact with the array of electrodes,

applying a potential to selected electrodes where synthesis is to occur for the second structure, thereby concentrating the second enzyme and the second structure at those selected sites, thereby coupling the second structure to the first structure, and

repeating the steps of providing the first solution for deblocking, applying a potential, applying a next solution with the next structure to be coupled and an enzyme to effect the coupling, and applying the potential to couple the next structure to the existing structure, to form the complex structures.

208. The method of claim 207 wherein the first structure is a nucleotide.

209. The method of claim 208 wherein the first structure is a blocked nucleotide comprising A, T, G or C.

210. The method of claim 207 whereby the first structure blocking group is a 3' phosphate ester.

211. The method of claim 207 wherein the enzyme in the first solution is a 3' phosphatase.

212. The method of claim 207 wherein the second structure is a blocked nucleotide comprising A, T, G or C.

213. The method of claim 207 wherein the second enzyme is a terminal transferase.

REMARKS

Claims 95-213 have been added to more fully cover applicant's disclosed invention regarding electronic synthesis. The title has been amended to conform to the claims. Claims 142-156 correspond to claims 15, 18, 19-23, 27, 28, 30-32, 35, 40 and 43 of U.S. Patent No. 6,093,302.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned **"Version with markings to show changes made."**

Respectfully submitted,

LYON & LYON LLP

Dated: July 24, 2001

By: ______________________
David Murphy
Reg. No. 31,125

DBM/dnd
633 West Fifth Street, Suite 4700
Los Angeles, California 90071-2066
(949) 567-2300 or (213) 489-1600

"Version with markings to show changes made"

In the Title:

Please change the title to Methods for Electronic Synthesis of Complex Structures.

In the Specification:

At Page 1, line 1, the following was added:

RELATED APPLICATION INFORMATION

This application is a continuation of U.S. Serial No. 09/490,965, filed January 24, 2000, which is a continuation of U.S. Serial No. 08/271,882, filed July 7, 1994, now issued as U.S. Patent No. 6,017,696, which is a continuation-in-part of U.S. Serial No. 08/146,504, filed November 1, 1993, now issued as U.S. Patent No. 5,605,662.

In the Claims:

Claims 1-94 have been cancelled.

Claims 95-213 have been added.

95. A method for electronic synthesis of a plurality of complex structures on a substrate, comprising the steps of:

providing a substrate having a plurality of controllable electrodes supported by the substrate,

providing first structures coupled to the electrodes, the structures having a blocked functional group,

providing a solution in contact with the array of electrodes,

applying a potential to selected electrodes where synthesis is to occur in order to cause deblocking of the first structure,

reacting a second structure with the deblocked first structure, and

repeating the steps of deblocking and reacting another structure to form the plurality of complex structures.

96. The method of claim 95 wherein the complex structures include a nanostructure.

97. The method of claim 95 wherein the complex structure include a polymer.

98. The method of claim 95 wherein the polymer is a synthetic polymer.

99. The method of claim 95 wherein the polymer is a biopolymer.

100. The method of claim 99 wherein the biopolymer is a polynucleotide.

101. The method of claim 99 wherein the biopolymer is a peptide.

102. The method of claim 95 wherein the first structure is a nucleotide.

103. The method of claim 95 wherein the first structure is a nanostructure.

104. The method of claim 95 wherein the first structure is a monomer.

105. The method of claim 95 wherein the first structure is an amino acid.

106. The method of claim 95 wherein the first structure is a chemically reactive moeity.

107. The method of claim 95 wherein the electrodes have terminal portions formed in an array.

108. The method of claim 95 wherein the synthesis of the plurality of complex structures occurs without mechanical movement of electrodes.

109. The method of claim 95 further including providing a layer of material disposed adjacent the electrodes.

110. The method of claim 109 wherein the layer couples the first structure to the electrode.

111. The method of claim 109 wherein the layer comprises a mesh structure.

112. The method of claim 109 wherein the layer comprises a porous structure.

113. The method of claim 109 wherein the layer comprises a lawn structure.

114. The method of claim 109 wherein the layer is a monolayer.

115. The method of claim 95 further including providing a scavenging substance.

116. The method of claim 115 wherein the scavenging substance is included in a layer of material disposed adjacent the electrode.

117. The method of claim 115 wherein the scavenging substance scavenges adverse materials.

118. The method of claim 117 wherein the adverse materials are produced in an electrochemical reaction.

119. The method of claim 109 wherein the layer is a permeation layer.

120. The method of claim 109 further including a first structure coupled to the layer.

121. The method of claim 95 wherein the second structure is present at the time of deblocking of the first structure.

122. The method of claim 95 wherein the second structure is provided subsequent to the deblocking of the first structure.

123. The method of claim 95 wherein the application of the potential to the selected electrodes causes electrophoretic transport of charged reactants to where synthesis is to occur.

124. The method of claim 95 further including the step of providing a charged deblocking reagent which is selectively attracted adjacent an electrode.

125. The method of claim 124 wherein the charged deblocking reagent is electrophoretically transported to an electrode.

126. The method of claim 95 wherein the electrodes are formed directly on the substrate.

127. The method of claim 95 wherein the electrodes are round.

128. The method of claim 95 wherein the electrodes are planar.

129. The method of claim 95 wherein a second potential is applied to at least one other electrode to protect structures at selected locations.

130. The method of claim 129 wherein the protected selected structure is associated with the electrode having the second potential.

131. The method of claim 95 wherein the electrode array is in contact with a common solution.

132. The method of claim 95 wherein the sequence of the structure of the array is determined by selective activation of electrodes adjacent a common solution.

133. The method of claim 95 wherein the application of an electric field to the selected electrodes provides a local concentration of reagents, wherein the reagents activate the selected site.

134. The method of claim 133 wherein activation of the selected site includes deblocking of the selected site.

135. The method of claim 95 wherein the electric field causes increased local concentration of reagents at the sites where the sub-unit is to be coupled.

136. The method of claim 95 wherein the solution contains a phosphate buffer.

137. The method of claim 95 wherein the solution contains a citrate buffer.

138. The method of claim 95 wherein the solution contains a borate buffer.

139. The method of claim 95 wherein the solution contains a TRIS buffer.

140. The method of claim 95 wherein the solution contains a TBE buffer.

141. The method of claim 95 wherein the functional group is a chemical functional group.

142. A method for electronic synthesis of an array of separately formed polymers on a substrate, which comprises the steps of:

placing a buffering solution in contact with an array of electrodes that is proximate to a substrate surface, said surface being proximate to one or more molecules bearing at least one protected chemical functional group attached thereto,

selectively deprotecting at least one protected chemical functional group on at least one of said molecules;

bonding a first monomer having at least one protected chemical functional group to one or more deprotected chemical functional groups of said molecule;

selectively deprotecting a chemical functional group on the bonded molecule or another of said molecules bearing at least one protected chemical functional group;

bonding a second monomer having at least one protected chemical functional group to a deprotected chemical functional group of the bonded molecule or said other deprotected molecule; and

repeating the selective deprotection of a chemical functional group on a bonded protected monomer or a bonded protected molecule and the subsequent bonding of an additional monomer to said deprotected chemical functional group until at least two separate polymers of desired length are formed on the substrate surface.

143. A method according to claim 142, wherein said buffering solution is selected from borate buffers, citrate buffers, and phosphate buffers.

144. A method according to claim 142, wherein said buffering solution is present in a concentration of at least 0.01 mM.

145. A method according to claim 142, wherein the concentration of the buffering solution ranges from 0.1 to 100 mM.

146. A method according to claim 142, wherein said monomers are amino acids.

147. A method according to claim 142, wherein said molecules are linker molecules or monomers.

148. A method according to claim 142, wherein said molecules are attached to a layer of material overlaying said substrate surface.

149. A method according to claim 142, wherein said substrate is formed from at least one material selected from semiconductors, glass, ceramics and polymers.

150. A method according to claim 142, wherein said array of electrodes comprises at least 100 electrodes.

151. A method according to claim 150, wherein said array of electrodes comprises a matrix having hundreds of thousands of electrodes.

152. A method according to claim 142, wherein each of the electrodes in said array ranges in diameter from less than 0.5 micron to about 200 microns.

153. A method according to claim 142, wherein the electrodes of said array are formed from platinum or palladium.

154. A method according to claim 142, which further comprises an additional bonding step wherein a pre-formed molecule is bonded to a deprotected chemical functional group on one or more of said molecules or monomers.

155. The method according to claim 142 wherein the monomer is a nucleotide.

156. A method according to claim 142 wherein a structure which scavenges adverse materials produced in an electrolysis reaction is situated proximate to one or more of said electrodes.

157. A method for electronically controlled synthesis of a plurality of complex structures on a substrate, comprising the steps of:

providing a substrate having a plurality of controllable electrodes supported by the substrate and covered with a non-insulating layer,

providing first structures coupled to the electrodes, the structures having a protected functional group,

providing a solution in contact with the array of electrodes supported by the substrate,

applying a potential to selected electrodes where synthesis is to occur,

reacting a second structure with the first structure, and

repeating the step of applying a potential and reacting a subsequent structure to form the complex structures, the synthesis of the array of structures occuring without mechanical movement.

158. The method of claim 157 wherein the activating of the selected site includes the deblocking of a protected reaction group.

159. The method of claim 157 wherein the complex structures include a nanostructure.

160. The method of claim 157 wherein the complex structure include a polymer.

161. The method of claim 157 wherein the polymer is a synthetic polymer.

162. The method of claim 157 wherein the polymer is a biopolymer.

163. The method of claim 162 wherein the biopolymer is a polynucleotide.

164. The method of claim 162 wherein the biopolymer is a peptide.

165. The method of claim 157 wherein the first structure is a nucleotide.

166. The method of claim 157 wherein the first structure is a nanostructure.

167. The method of claim 157 wherein the first structure is a monomer.

168. The method of claim 157 wherein the first structure is an amino acid.

169. The method of claim 157 wherein the first structure is a chemically reactive moeity.

170. The method of claim 157 wherein the electrodes have terminal portions formed in an array.

171. The method of claim 157 wherein the synthesis of the plurality of complex structures occurs without mechanical movement of electrodes.

172. The method of claim 157 further including providing a layer of material disposed adjacent the electrodes.

173. The method of claim 172 wherein the layer couples the first structure to the electrode.

174. The method of claim 172 wherein the layer comprises a mesh structure.

175. The method of claim 172 wherein the layer comprises a porous structure.

176. The method of claim 172 wherein the layer comprises a lawn structure.

177. The method of claim 172 wherein the layer is a monolayer.

178. The method of claim 157 further including providing a scavenging substance.

179. The method of claim 178 wherein the scavenging substance is included in a layer of material disposed adjacent the electrode.

180. The method of claim 178 wherein the scavenging substance scavenges adverse materials.

181. The method of claim 180 wherein the adverse materials are produced in an electrochemical reaction.

182. The method of claim 172 wherein the layer is a permeation layer.

183. The method of claim 172 further including a first structure coupled to the layer.

184. The method of claim 157 wherein the second structure is present at the time of deblocking of the first structure.

185. The method of claim 157 wherein the second structure is provided subsequent to the deblocking of the first structure.

186. The method of claim 157 wherein the application of the potential to the selected electrodes causes electrophoretic transport of charged reactants to where synthesis is to occur.

187. The method of claim 157 further including the step of providing a charged deblocking reagent which is selectively attracted adjacent an electrode.

188. The method of claim 187 wherein the charged deblocking reagent is electrophoretically transported to an electrode.

189. The method of claim 157 wherein the electrodes are formed directly on the substrate.

190. The method of claim 157 wherein the electrodes are round.

191. The method of claim 157 wherein the electrodes are planar.

192. The method of claim 157 wherein a second potential is applied to at least one other electrode to protect structures at selected locations.

193. The method of claim 192 wherein the protected selected structure is associated with the electrode having the second potential.

194. The method of claim 157 wherein the electrode array is in contact with a common solution.

195. The method of claim 157 wherein the sequence of the structure of the array is determined by selective activation of electrodes adjacent a common solution.

196. The method of claim 157 wherein the application of an electric field to the selected electrodes provides a local concentration of reagents, wherein the reagents activate the selected site.

197. The method of claim 196 wherein activation of the selected site includes deblocking of the selected site.

198. The method of claim 157 wherein the electric field causes increased local concentration of reagents at the sites where the sub-unit is to be coupled.

199. The method of claim 157 wherein the solution contains a phosphate buffer.

200. The method of claim 157 wherein the solution contains a citrate buffer.

201. The method of claim 157 wherein the solution contains a borate buffer.

202. The method of claim 157 wherein the solution contains a TRIS buffer.

203. The method of claim 157 wherein the solution contains a TBE buffer.

204. The method of claim 157 wherein the functional group is a chemical functional group.

205. A method for electronically controlled synthesis of an array of structures supported on a substrate, the synthesized structures including a predetermined sequence of sub-units, comprising the steps of:

providing an plurality of electrodes, the electrodes being supported by the substrate,

providing a buffer in contact with the electrodes,

applying an electric field to selected electrodes wherein a sub-unit is to be included within the structures of the array and applying a second electric field to at least certain other selected electrodes to protect the structures within the array where the said sub-unit is not to be included, and

coupling a selected sub-unit to the said selected locations within the array wherein the sub-unit is to be included.

206. The method of claim 205 wherein the synthesis of the array of structures occurs without mechanical movement of the electrodes.

207. A method for electronically controlled synthesis of a plurality of complex structures on a substrate, comprising the steps of:

providing a substrate having a plurality of controllable electrodes supported by the substrate and covered with a non-insulating layer,

providing first structures coupled to the electrodes, the structures having a blocking group,

providing a first solution in contact with the array of electrodes supported by the substrate containing an enzyme for selective removal of the blocking group,

applying a potential to selected electrodes where synthesis is to occur, thereby concentrating the enzyme at those selected sites,

providing a second solution containing a second enzyme for coupling and a second structure having a blocking group in contact with the array of electrodes,

applying a potential to selected electrodes where synthesis is to occur for the second structure, thereby concentrating the second enzyme and the second structure at those selected sites, thereby coupling the second structure to the first structure, and

repeating the steps of providing the first solution for deblocking, applying a potential, applying a next solution with the next structure to be coupled and an enzyme to effect the coupling, and applying the potential to couple the next structure to the existing structure, to form the complex structures.

208. The method of claim 207 wherein the first structure is a nucleotide.

209. The method of claim 208 wherein the first structure is a blocked nucleotide comprising A, T, G or C.

210. The method of claim 207 whereby the first structure blocking group is a 3' phosphate ester.

211. The method of claim 207 wherein the enzyme in the first solution is a 3' phosphatase.

212. The method of claim 207 wherein the second structure is a blocked nucleotide comprising A, T, G or C.

213. The method of claim 207 wherein the second enzyme is a terminal transferase.